

PCT COOPERATION TREATY

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NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE
in its capacity as elected Office

Date of mailing (day/month/year) 25 April 2001 (25.04.01)	
International application No. PCT/US00/20013	Applicant's or agent's file reference 18010-0061WP
International filing date (day/month/year) 21 July 2000 (21.07.00)	Priority date (day/month/year) 23 July 1999 (23.07.99)
Applicant NOSKY, Bruce, J. et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

22 February 2001 (22.02.01)

☐ in a notice effecting later election filed with the International Bureau on:2. The election ☒ was☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Claudio Borton Telephone No.: (41-22) 338.83.38
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TENT COOPERATION TREA Y

PCT

NOTIFICATION OF THE RECORDING
OF A CHANGE(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

YOUNG, Leona, G.
Kilpatrick Stockton LLP
2400 Monarch Tower
3424 Peachtree Road, N.E.
Atlanta, GA 30326
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year) 28 January 2002 (28.01.02)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference 18010-0061WP	
International application No. PCT/US00/20013	International filing date (day/month/year) 21 July 2000 (21.07.00)

1. The following indications appeared on record concerning:		
<input checked="" type="checkbox"/> the applicant	<input type="checkbox"/> the inventor	<input type="checkbox"/> the agent <input type="checkbox"/> the common representative
Name and Address BIONICHE LIFE SCIENCES INC. 383 Sovereign Road London, Ontario N6M 1A3 Canada	State of Nationality CA	State of Residence CA
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:		
<input type="checkbox"/> the person	<input type="checkbox"/> the name	<input checked="" type="checkbox"/> the address <input type="checkbox"/> the nationality <input type="checkbox"/> the residence
Name and Address BIONICHE LIFE SCIENCES INC. 231 Dundas Street E. Belleville Ontario K8N 1E2 Canada	State of Nationality CA	State of Residence CA
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
3. Further observations, if necessary:		
4. A copy of this notification has been sent to:		
<input checked="" type="checkbox"/> the receiving Office	<input type="checkbox"/> the designated Offices concerned	
<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned	
<input type="checkbox"/> the International Preliminary Examining Authority	<input type="checkbox"/> other:	

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Anne KARKACHI
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

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PATENT COOPERATION TREATY

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INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 18010-0061WP	FOR FURTHER ACTION		see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
International application No. PCT/US 00/ 20013	International filing date (day/month/year) 21/07/2000	(Earliest) Priority Date (day/month/year) 23/07/1999	
Applicant BIONICHE LIFE SCIENCES INC. et al.			

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 97/20855

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 A23K1/16 A23K1/18 A61K39/39

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A23K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 93 00017 A (UNIV LEEDS) 7 January 1993 see page 1, paragraph 1 - page 4, paragraph 3 see page 5, last paragraph - page 26, last paragraph see claims 1-11	1, 4, 36-40
Y	---	16-22, 34, 35
Y	EP 0 285 441 A (INT MINERALS & CHEM CORP) 5 October 1988 see page 5, line 45 - page 6, line 2 see claims 1-7, 12-18 --- -/--	16-22, 34, 35

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

20 March 1998

Date of mailing of the international search report

02/04/1998

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Dekeirel, M

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 97/20855

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2 620 274 A (DAN LEWIS ET AL.) 2 December 1952 see column 1, line 45 - column 3, line 35 see claims 1-7 see claims 1-16 ---	1,3,4, 36-38,40
X	US 2 946 722 A (W.H. HOFFMAN ET AL.) 26 July 1960 see column 6, line 57 - column 11, line 27 ---	1,2,4, 36-38,40
X	US 1 867 063 A (C.C. DAWE) 12 July 1932 see the whole document ---	1,3,36
X	EP 0 158 075 A (BAYER AG) 16 October 1985 see page 7, line 20 - page 16, line 3 see example A see claims 1-7,9 ---	1
P,X	WO 96 39862 A (NOVUS INT INC) 19 December 1996 see the whole document ---	1-5, 11-13, 15,36-40
A	WO 96 27666 A (COMMW SCIENT IND RES ORG ;LOWENTHAL JOHN WILLIAM (AU); YORK JENNIF) 12 September 1996 see examples 24-26 see claims 66-107,113 ---	16,18,34
A	EP 0 592 220 A (EISAI CO LTD) 13 April 1994 see page 3, line 9 - page 5, line 35 see page 6, line 36 - page 9, line 19 see page 20, line 42 - page 21, line 57 see page 25, line 1 - page 26, line 3 see claims 1-12 ---	16,18,34
A	US 5 217 740 A (LANTER KENT J) 8 June 1993 cited in the application see the whole document ---	1,36
A	D.H. THORNE ET AL.: "Automated high moisture diet feeding system for laying hens" POULTRY SCIENCE, vol. 68, no. 8, 1989, US, pages 1114-1117, XP002013290 see the whole document ---	1,36
	-/--	

INTERNATIONAL SEARCH REPORT

national Application No

PCT/US 00/20013

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K35/74 A61P37/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K A23K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

BIOSIS, EPO-Internal, WPI Data, PAJ, MEDLINE, CHEM ABS Data, EMBASE, SCISEARCH

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	VAN KAMPEN KENT R: "Immunotherapy and cytokines." SEMINARS IN VETERINARY MEDICINE AND SURGERY (SMALL ANIMAL), vol. 12, no. 3, 1997, pages 186-192, XP000979433 ISSN: 0882-0511 the whole document, especially page 188 column 1 lines 18-25 and page 191 lines 47-60 ---	1-14
T	VETREPHARM: "The Science Behind Immunoboost" IMMUNOBOOST, XP002159576 Retrieved from the Internet: <URL:http://www.vetrepharm.com/immuno/science.htm> 'retrieved on 2001-02-06! ---	1-14
-/--		

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- * & * document member of the same patent family

Date of the actual completion of the international search

6 February 2001

Date of mailing of the international search report

19/02/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Stein, A

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/20013

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 98 24327 A (NOVUS INT INC) 11 June 1998 (1998-06-11) page 4, line 13 -page 5, line 7 page 18, line 21 -page 19, line 25 claims 1,4,5,7,18,22,23,25,34,36,38 ---	1-14
A	WO 95 05837 A (VETREPHARM INC) 2 March 1995 (1995-03-02) the whole document ---	1-14
A	WO 94 16727 A (VETREPHARM INC) 4 August 1994 (1994-08-04) the whole document -----	1-7

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INTERNATIONAL SEARCH REPORT

Information on patent family members

Int. Application No

PCT/US 00/20013

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9824327 A	11-06-1998	US 5976580 A	02-11-1999
		AU 5258598 A	29-06-1998
		BR 9713996 A	29-02-2000
		EP 0944333 A	29-09-1999
WO 9505837 A	02-03-1995	AU 7488794 A	21-03-1995
		AU 8943498 A	24-12-1998
		CA 2170142 A	02-03-1995
		EP 0714305 A	05-06-1996
		US 5632995 A	27-05-1997
WO 9416727 A	04-08-1994	AT 179333 T	15-05-1999
		AU 691797 B	28-05-1998
		AU 5968094 A	15-08-1994
		BR 9406496 A	02-01-1996
		CA 2154689 A	04-08-1994
		CN 1118574 A	13-03-1996
		DE 69418183 D	02-06-1999
		DE 69418183 T	16-12-1999
		DK 681479 T	08-11-1999
		EP 0681479 A	15-11-1995
		JP 8508976 T	24-09-1996
		NZ 261094 A	27-04-1998
		US 5759554 A	02-06-1998

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(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



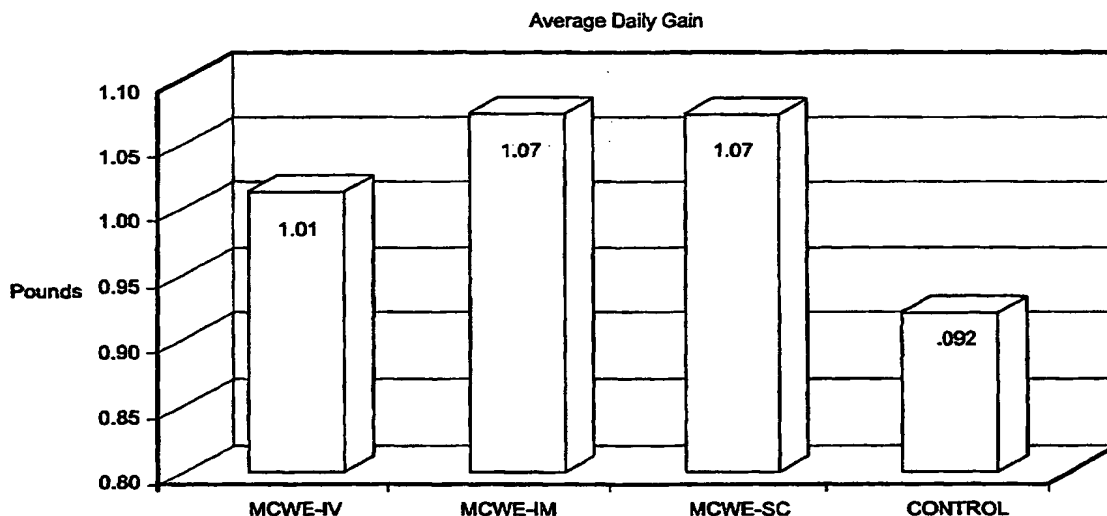
(43) International Publication Date
1 February 2001 (01.02.2001)

PCT

(10) International Publication Number
WO 01/07080 A2

- (51) International Patent Classification⁷: **A61K 39/00**
- (21) International Application Number: **PCT/US00/20013**
- (22) International Filing Date: **21 July 2000 (21.07.2000)**
- (25) Filing Language: **English**
- (26) Publication Language: **English**
- (30) Priority Data:
60/145,314 23 July 1999 (23.07.1999) **US**
- (71) Applicant (for all designated States except US):
BIONICHE LIFE SCIENCES INC. [CA/CA]; 383 Sovereign Road, London, Ontario N6M 1A3 (CA).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **NOSKY, Bruce, J. [US/US]; Post Office Box 230, Hull, GA 30646 (US). PITTS, Robert, E. [US/US]; 309 Sandstone Drive, Athens, GA 30605 (US). ROGAN, Dragan, R. [CA/CA]; 138 Saddy Avenue, London, Ontario N5V 4N1 (CA).**
- (54) Agents: **YOUNG, Leona, G. et al.; Kilpatrick Stockton LLP, 2400 Monarch Tower, 3424 Peachtree Road, N.E., Atlanta, GA 30326 (US).**
- (81) Designated States (national): **AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.**
- (84) Designated States (regional): **ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).**
- Published:
— Without international search report and to be republished upon receipt of that report.
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **METHOD FOR ENHANCING PRODUCTION PERFORMANCE IN AN ANIMAL**



(57) Abstract: The present invention provides a method of activating the immune system of a newborn animal and enhancing production performance of the animal comprising administering to the newborn animal an effective amount of a *Mycobacterium phlei* cell wall extract (MCWE), thereby activating the immune system of the animal and enhancing production performance of the animal.

WO 01/07080 A2

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PATENT COOPERATION TREATY

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REC'D 16 OCT 2001

WIPO PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

14

Applicant's or agent's file reference 18010-0061WP	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US00/20013	International filing date (day/month/year) 21/07/2000	Priority date (day/month/year) 23/07/1999
International Patent Classification (IPC) or national classification and IPC A61K39/00		
Applicant BIONICHE LIFE SCIENCES INC. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 7 sheets, including this cover sheet.

- ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 6 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 22/02/2001	Date of completion of this report 10.10.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Herrero, M Telephone No. +49 89 2399 8542 

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/20013

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1,3-5,7-15 as originally filed

2,6 as received on 19/09/2001 with letter of 17/09/2001

Claims, No.:

1-31 as received on 19/09/2001 with letter of 17/09/2001

Drawings, sheets:

1/5-5/5 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

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**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US00/20013

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
☒ claims Nos. 1-14, 16, 17-24(part), 25, 26 and 29-31(part) with respect to industrial applicability.

because:

- ☒ the said international application, or the said claims Nos. 1-14, 16, 17-24(part), 25, 26 and 29-31(part) relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the standard.
☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/20013

1. Statement

Novelty (N)	Yes:	Claims	1-31
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-31
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	15, 17-24 (part), 27, 28, 29-31(part)
	No:	Claims	

2. Citations and explanations **see separate sheet**

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

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SECTION III

Claims 1-14, 16, 17-24 (in part), 25, 26 and 29-31 (in part) relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

SECTION V

2. CITATIONS AND EXPLANATIONS

2.1 The following documents have been considered for the purposes of this report:

D1: K.R. Van Kampen (1997) Seminars in Veterinary Medicine and Surgery
(Small Animal) 12:186-192

D3: WO 94/16727 (equivalent to US-A-5759554, cited in the application)

2.2 This preliminary examination report takes into account the content of the Applicants' letter of 17.09.01 in reply to the written opinion dated 17.07.01.

D1 reviews a number of veterinary products directed towards nonspecific stimulation of the immune system which are made from *Mycobacterium spp* cell walls or fractions thereof (see also the related statement on page 2, lines 5-10 of the present description). This nonspecific immune stimulation (the prevalent mode of therapeutic use of immunomodulators) results in the activation of macrophages and the production of cytokines (e.g. IFN-gamma) by macrophages and T lymphocytes (cf page 187, paragraph bridging left and right columns). The activation of specific or nonspecific immunocellular functions, e.g. of cytotoxic lymphocytes, neutrophils, monocytes and T-helper cells may additionally occur (cf page 187, right column, second paragraph). Among the immunostimulant products derived from *Mycobacterium spp* cell walls extracts (MCWE), D1 makes reference to Immunoboost K, a licensed product for use in calves with scours

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caused by infection with *Escherichia coli*, namely for the one time immunotherapeutic treatment for the reduction of clinical signs and mortality associated with *E. coli* (K99) diarrhea. Treatment with Immunoboost K causes macrophage activation, cytokine production and increased numbers and activation of T lymphocytes (cf page 188, left column, lines 18-25 and page 191, bottom lines).

D3 describes the use of MCWE for the general stimulation of the immune system of an animal or human so that the individual's own immune system is capable of rapidly eliminating a wide variety of disorders, e.g. neutralize or abort an infection or retard or eliminate the growth of a cancer.

The intended uses of mycobacterial cell wall extracts (MCWE) described and claimed in the present application, which involve the administration of such mycobacterial extracts to a newborn animal within the first 24 hours, 4 days or 28 days of life for the purposes of activating the immune system of the newborn animal or enhancing production performance of the animal, would appear to be neither anticipated nor suggested by the teachings of either D1 or D3, taken into consideration alone or in combination, insofar as the person skilled in the art would not obviously consider that early administration of such mycobacterial extracts within the first 28 days of life would provide long lasting effects on immune function or long lasting changes in production performance as those hereby disclosed (cf Examples 2 and 3).

In line with the foregoing, present Claims 1-31 seem to relate to subject-matter that is novel and inventive over the available prior art and therefore satisfy the criteria set forth in Art. 33(2) and (3) PCT.

2.3 Industrial applicability (Art. 33(4) PCT)

For the assessment of the present Claims 1-14, 16, 17-24(part) and 25-31 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as

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industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

SECTION VII

1. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in document D1, is not mentioned in the description, nor is this document identified therein.
2. The term "Tween" (page 10, line 11) appears to be a registered trade mark, but has not been acknowledged as such.
3. The expression "hereby incorporated by reference" in respect of prior art documents on page 9, lines 34-35 leads to a doubt as to whether the requirements of the description being self-contained are satisfied (see PCT Guidelines C-II, 4-17).

SECTION VIII

The statements in the description on page 9, lines 26-30 and page 15, lines 26-29 imply that the subject-matter for which protection is sought may be different to that defined by the claims, thereby resulting in lack of clarity (Article 6 PCT) when used to interpret them (see also the PCT Guidelines, III-4.3a).

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International Application No

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(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
1 February 2001 (01.02.2001)

PCT

(10) International Publication Number
WO 01/07080 A3

- (51) International Patent Classification⁷: **A61K 35/74**, **A61P 37/04**
- (21) International Application Number: **PCT/US00/20013**
- (22) International Filing Date: **21 July 2000 (21.07.2000)**
- (25) Filing Language: **English**
- (26) Publication Language: **English**
- (30) Priority Data:
60/145,314 **23 July 1999 (23.07.1999)** **US**
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- (81) Designated States (*national*): **AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.**
- (84) Designated States (*regional*): **ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).**
- Published:**
— *with international search report*
- (88) Date of publication of the international search report:
16 August 2001

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **METHOD FOR ENHANCING PRODUCTION PERFORMANCE IN AN ANIMAL**

(57) Abstract: The present invention provides a method of activating the immune system of a newborn animal and enhancing production performance of the animal comprising administering to the newborn animal an effective amount of a *Mycobacterium phlei* cell wall extract (MCWE), thereby activating the immune system of the animal and enhancing production performance of the animal.

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**REPLACED BY
ART 34 AMDT**

Various biological and chemical immunomodulators have been used to stimulate the immune system to minimize the impact of disease in animals, including humans. These include, but are not limited to, opioid peptides, thymosins, glucocorticoids, cytokines, interferons, levamisole, isoprinosine, poynucleotides and microbial products. Microbial products that have been used as immunomodulators include, but are not limited to, heat killed or formaldehyde treated suspensions of *Priopionibacterium acnes*, microbial polysaccharides, lipopolysaccharides, protein-bound polysaccharides, muramyl-dipeptide, lipid A and *Mycobacterium phlei* cell wall extract (U.S. Patent. No. 4,744,984; U.S. Patent No. 5,579,554).

Domestic food animals are particularly susceptible to infectious disease during the first year of life and more particularly during the neonatal period. Among calves over 70% of deaths that occur during the first year of life occur during the neonatal period when their immune system is functionally immature (Radostits et al. 1985. Herd Health. W.B. Saunders, Philadelphia PA. pgs. 116-1400). Functional immaturity of the immune system includes, but is not limited to, sub-optimal neutrophil function (Hauser et al. 1986. Am. J. Vet. Res. 47:152-153), decreased complement activity (Renshaw et al. 1978. Immunology 34:801-805), poor induction of delayed hypersensitivity reactions (Woodward et al. 1979. Am. J. Vet. Res. 40:636-644), low levels of interleukin (IL)-2 production (Griebel et al. 1987. Can. J. Vet. Res. 51:428-435) and weak lymphocyte proliferative responses (Rossi et al. 1979. Am. J. Vet. Res. 40:576-579; Rossi et al. 1981. Am. J. Vet. Res. 27:1369-1370).

Because of the many diseases to which animals are vulnerable and because, during the newborn and neonatal periods, some of these diseases are exacerbated by an immature immune system, there is a need for a novel method for activating the immune system to enhance disease resistance, especially during the newborn and neonatal periods, and, thereby, to increase production performance in these animals.

This method should be relatively inexpensive to prepare, easy to administer and suitable for use in all animals. Moreover, its activity should remain stable over time, be reproducible among preparations, be effective at dose regimens associated with minimal toxicity, be safe for the consumer and be acceptable to all segments of the population.

SUMMARY OF THE INVENTION

The present invention satisfies the above needs by providing a method for activating the immune system of a newborn animal to enhance

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BRIEF DESCRIPTION OF THE FIGURES

FIG. 1. CD25⁺CD4⁺ T-lymphocytes/ml (A) and MHC Class II⁺CD4⁺ T-lymphocytes/ml (B) in blood obtained on day 4 from calves treated within 24 hours of birth (day 0) with MCWE-IV, MCWE-SC and saline-SC (control). Values are for individual animals and bars represent mean values for each group (n=4).

FIG. 2. MHC Class II⁺ monocytes/ml in blood obtained on day 4 from calves treated within 24 hours of birth (day 0) with MCWE-IV, MCWE-SC and saline-SC (control). Values are for individual animals and bars represent mean values for each group (n=4).

FIG. 3. INF γ production by WBCs obtained on day 4 from calves treated within 24 hours of birth (day 0) with MCWE-IV, MCWE-SC and saline-SC (control). Values are for individual animals and bars represent mean values for each group (n=4).

FIG. 4. Average daily weight gain among calves treated, within 24 hours of birth (day 0), with MCWE-IV, MCWE-IM, MCWE-SC and no MCWE (control).

FIG. 5. Average number of days, during a 71-78 day period, that treatment was necessary to maintain the health of animals who, within 24 hours of birth (day 0), received MCWE-IV, MCWE-IM, MCWE-SC or no MCWE (control).

FIG. 6. Costs, during a 71-78 day period, associated with the treatments necessary to maintain the health of animals who, within 24 hours of birth (day 0), received MCWE-IV, MCWE-IM, MCWE-SC or no MCWE (control).

DETAILED DESCRIPTION OF THE INVENTION

The present invention provides a method for activating the immune system of a newborn animal to enhance production performance of the animal comprising administering to the newborn animal an effective amount of MCWE, thereby activating the immune system of the newborn animal to enhance production performance. More particularly, the present invention provides a method for activating the immune system of a newborn animal to enhance production performance of the animal comprising administering to the newborn animal within 24 hours of birth an effective amount of MCWE, thereby activating the immune system of the newborn animal to enhance production performance.

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CLAIMS

We claim:

- 5 1. A method of activating the immune system of a newborn animal comprising administering to the newborn animal an effective amount of a *Mycobacterium phlei* cell wall extract (MCWE), thereby activating the immune system of the newborn animal.
- 10 2. The method of claim 1, wherein the MCWE is administered to activate the white blood cells of the immune system.
3. The method of claim 2, wherein the white blood cells are selected from the group consisting of T-lymphocytes and monocytes.
- 15 4. The method of claim 3, wherein the T-lymphocytes are CD4⁺ T lymphocytes.
5. The method of claim 4, wherein the CD4⁺ T-lymphocytes are selected from the group consisting of CD25⁺CD4⁺ T lymphocytes and MHC Class II⁺CD4⁺ T lymphocytes.
- 20 6. The method of claim 3, wherein the monocytes are MHC Class II⁺ monocytes.
- 25 7. The method of claim 2, wherein the white blood cells produce INF γ .
8. A method of enhancing production performance in an animal comprising administering to a newborn animal an effective amount of MCWE, thereby enhancing production performance of the animal.
- 30 9. The method of claim 8, wherein the enhancement of production performance is selected from the group consisting of an increase in the average daily weight gain of an animal, a decrease in the mortality of an animal, a decrease in the number of treatment days necessary to maintain the health of an animal, a decrease in the cost of treatment necessary to maintain the health of an animal and any combination thereof.
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10. The method of claim 1 and 8, wherein the newborn animal is less than 24 hours of age.
- 5 11. The method of claims 1 and 8, wherein the animal is a domestic food animal.
12. The method of claim 11, wherein the domestic food animal is selected from the group consisting of a calf, chick, piglet and lamb.
- 10 13. The method of claim 12, wherein the domestic food animal is the calf of a domestic cow.
- 15 14. The method of claim 13, wherein the domestic food animal is the chick of a common domestic chicken.

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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